

U.S.S.N. 10/521,868

Final Office Action mailed April 12, 2010

Amendment under 37 C.F.R. 1.116 filed August 5, 2010

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Remarks

To expedite prosecution, Applicants have amended claims 12, 13 and 14 to specifically refer to the exemplary algae species used in the Examples, namely *Chaetoceros gracilis* and *Skeletonema costatum*. Claims 1 and 2 previously directed to these two algae species have thus been cancelled without prejudice. Accordingly, no new matter has been introduced by the amendments and their entry is respectfully requested.

Rejections under 35 USC § 112

The Examiner rejected claims 1-6, and 11-12 as allegedly not complying with 35 U.S.C. §112, first paragraph written description requirement. The Examiner alleged that that the specification fails show that the Applicant was in possession of the invention at the time of filing. Specifically, the Examiner alleged that the Applicants have not shown possession of a method using any and all species under *Chaetocerotaceae* or *Skeletonemaceae*, because only one exemplary species has been used in the specification for each of these families.

Applicants respectfully disagree and submit that the rejection should be withdrawn for the following reasons.

The two exemplary species used in the experiments set forth in the specification are *Chaetoceros gracilis* and *Skeletonema costatum*. Claims 1 and 2 were drawn to these species specifically. Therefore, the rejection should not be applied to claims 1 or 2.

Also, Applicants have amended the claims to only apply to the two specifically exemplified species set forth in claims 1 and 2. To comply with the amendment, claims 1 and 2 have been canceled.

Accordingly, in view of the above, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph written description requirement, should be withdrawn.

Rejections under 35 USC § 103

The Examiner rejected claims 1-6 and 12-14 under 35 USC 103(a) over previously cited McGinnis, taken with a newly cited Reitan et al. (Journal of Phycology 30(6): 972-979,

1994)(“Reitan”), and previously cited Dempster and Taguchi. Specifically, the Examiner alleged that Reitan describes a “semi continuous” culture for the production of PUFAs, and thus, any optimization to the claimed method which also uses a semi-continuous system in view of Reitan and the teachings of McGinnis, Dempster and Taguchi is obvious.

Applicants respectfully disagree and submit that the rejection should be withdrawn for the following reasons.

The Examiner interpreted all references describing methods wherein “at least some cells are in exponential growth phase.” As already discussed in the prior response, this interpretation is incorrect because the claims refer to “culture” as a whole, not individual cells. The term “exponential growth phase” of an algae culture has a well-known meaning in the art as referring to the growth profile of a culture - not to the growth of any particular cell within that culture (see also Exhibit A, attached herewith). Moreover, the claims specifically recite “culture” as opposed to “at least some diatoms were in exponential phase.”

The Examiner further continues to equal the terms “**at the end** of exponential phase” to “**after the end** of exponential phase”, thereby incorrectly construing the claims. There is a significant difference in the phrases, “at the end” of exponential phase refers to a culture that has not yet entered a stationary growth phase, whereas, “after the end” of exponential phase, the term the Examiner himself is using, refers to the stationary growth phase, which is not what is claimed. In view of the well known growth phases of algae, the Examiner’s contention regarding the teaching of the prior art is incorrect. All the cited references specifically teach cell manipulation **at the stationary phase, not at the end of exponential growth phase** which occurs before the stationary phase. Claim language does **not include the term “after”** the exponential phase, but specifically **refers to the point “at” the end** of the exponential phase. These terms give an entirely different meaning to the scope of the claims. Thus, none of the prior art can be read on the current claims. Moreover, specification mentions at least twice that the deprivation is to be applied “at the end of their exponential growth phase, and have thus attained a maximum concentration” (see page 4, lines 7 and 8, and further lines 23-24). From the teaching of the application, it is clear for a person skilled in the art that if one wished to have a maximum concentration of cells, one will wait

until the end of the exponential phase, but not until **the stationary phase where cells start dying**, and thus the cell concentration will start dropping.

For example, as already discussed earlier, McInnis specifically taught a deprivation of nitrogen at day 4. Page 20, second column of McInnis, shows that the **cells were at the stationary phase, not at the end of exponential phase** which is what is claimed. McGinnis Figure 3, by day-two the culture had reached the peak of exponential growth, and by day-four (as indicated by the horizontal line evidencing that cell growth rate equaled cell death rate in the Figure attached to the previous amendment), the culture had passed into stationary phase. Indeed, McGinnis specifically states that “By Day 3, **growth reached stationary phase.**” (page 21, col. 1). Accordingly, as stated before, nothing in McInnis teaches, suggests or lets a skilled artisan to expect success for a method that uses cell in exponential rather than stationary phase.

Taguchi does not cure the deficiency in McInnis, namely, also Taguchi does not teach that the culture is at the end of exponential phase. Rather, Taguchi teaches, at Fig. 1, deprivation test was conducted **at the stationary phase and not at the end of the exponential phase** (see positioning of arrows in Fig. 1 of Taguchi). In addition, the effect is measured using total lipid content and nothing is mentioned regarding enrichment of PUFA.

The newly cited Reitan also does not cure the deficiency in McInnis because it does not teach adding a growth limiting factor at the end of the exponential growth phase. Reitan only teaches comparative study of nutrient limitation on fatty acids and lipid content in various species. The conclusion is that PUFA are diminished, which is also contrary to the findings in the present invention.

Dempster fails to cure the deficiency in McInnis because also the cultures in Dempster are in stationary growth phase, as is clear from the nitrogen stress which is conventionally applied at the stationary phase.

By contrast, as taught be the instant application and recited in the claims: “After 6-7 days ... the algae **cultures** were at the end of their exponential growth phase. **Only at the end of the**

exponential growth phase were the algae stressed..." (page 4, lines 6-10 of the specification, emphasis added)

Accordingly, the combination of the cited references does not teach all the elements of the claims, namely, the element of applying at least one growth limiting factor **at the end of exponential growth phase**, is not taught or suggested in any of the cited references. There is also no indication that silicate deprivation initiated at the end of exponential growth phase is critical for the result of an increase in Omega-3 fatty acid production in the claimed cultures of *Chaetoceros gracilis* and *Skeletonema costatum* algae species now claimed. Therefore, the cited references do not combine to provide for the claimed invention.

Furthermore, the inventors have also found that the application of a growth limiting factor to any diatomaceous algae would not necessarily systematically result in an increase in PUFA production (see, attached Exhibit B). Exhibit B shows tests that were performed on *Thalassiosira pseudonana*. The results following silica deprivation show that there is no significant accumulation and/or specific increase/production of PUFA (see specifically Table 1 and Figs. 2 and 3). None of the cited references used the now specifically claimed species, namely, *Chaetoceros gracilis* and *Skeletonema costatum* algae cells. In view of the additional results by the inventors, the teachings of the prior art references regarding other than the *Chaetoceros gracilis* and *Skeletonema costatum* algae cells cannot be predictive of the invention as now claimed. Thus, in view of Exhibit B, Dempster, McGinnis and Reitan cannot be considered, alone or in combination, as teaching or suggesting the present method, or allowing one to expect success with the method as presently claimed. Without the teachings of Dempster, McGinnis and Reitan, Taguchi alone does not teach all the elements of the invention, namely, it does not teach a process of culturing algae for production of PUFA. Also, as indicated above, also in Taguchi, the deprivation test was conducted at the stationary phase and not at the end of the exponential phase

In view of the above, Applicants respectfully submit that the rejection under 35 U.S.C. 103(a) should be withdrawn.

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Conclusion

In view of the foregoing, Applicants respectfully submit that all the pending claims are in condition for allowance. At minimum, the amendments to the claims and the additional evidence presented into the file will reduce issues on appeal. Early and favorable action is requested.

The Commissioner is hereby authorized to charge any fees, such as additional claims fees, and credit any overpayments that may be due in connection with this submission to Nixon Peabody LLP Deposit Account No. 50-0850.

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Respectfully submitted,

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